Occupation and risk of primary Fallopian tube carcinoma in Nordic countries

A Riska[1], JI Martinsen[2], K Kjaerheim[2], E Lynge[3], P Sparen[4], L Tryggvadottir[5], E Weiderpass[2,4,6,7], E Pukkala[8,9]

[1]Department of Obstetrics and Gynaecology, Helsinki University Central Hospital, Helsinki, Finland

[2]Cancer Registry of Norway, Oslo, Norway

[3]University of Copenhagen, Denmark

[4]Department of Epidemiology and Biostatistics, Karolinska Institute, Stockholm, Sweden

[5]Icelandic Cancer Registry, Reykjavik, Iceland

[6]Samfundet Folkhälsan, Helsinki, Finland

[7]Department of Community Medicine, University of Tromsø, Tromso, Norway

[8]Finnish Cancer Registry, Institute for Statistical and Epidemiological Cancer Research, Helsinki, Finland

[9]School of Public Health, University of Tampere, Tampere, Finland

Abstract

The aetiology of primary Fallopian tube carcinoma (PFTC) is poorly understood. Occupational exposures may contribute to PFTC risk. We studied incidence of PFTC in occupational categories in the Nordic female population aged 30-64 years during the 1960, 1970, 1980/1981 and/or 1990 censuses in Denmark, Finland, Iceland, Norway and Sweden. Standardized incidence ratios (SIRs) for the years following inclusion in the study up to 2005 were calculated for 53 occupations; the expected numbers of cases were based on PFTC incidence in the national populations. Altogether 2206 PFTC cases were detected during follow up via data linkages with the Nordic cancer registries. Significantly increased risks of PFTC were observed for smelting workers (SIR 3.99, 95% confidence interval 1.46-8.68,Obs=6), artistic workers (2.64, 1.44-4.43,Obs=14), hairdressers (2.18, 1.41-3.22,Obs=25), packers (1.62, 1.11-2.29,Obs=32), nurses (1.49, 1.14- 1.92,Obs=60), shop workers (1.25, 1.07-1.46,Obs=159) and clerical workers (1.20, 1.07-1.35,Obs=271) and these sustained over times and different Nordic countries. There was a non-significant increased risk for PFTC among welders, printers, painters and chemical process workers. The risk was significantly and consistently low for women working in farming (0.68, 0.47-0.95,Obs=34) and among economically inactive women (0.88, 0.82-0.94,Obs=833). The possible role of occupational exposures to the PFTC risks found in this study must be further evaluated in studies with a possibility to adjust for possible confounding factors, such as reproductive and life-style factors, which was not possible in our study.

Key words: Primary Fallopian tube carcinoma; occupation; standardized incidence ratio; Nordic; epidemiology, women, cohort, cancer

Introduction

Primary Fallopian tube carcinoma (PFTC) is a rare malignancy, comprising about 1% of all female genital tract cancers (1, 2). Studies from the United States indicated an incidence rate of 0.4/100,000 person-years in the 1980s; with the rate being higher in Caucasian women including Hispanics than in African Americans (3).The age-adjusted incidence of PFTC has been increasing during the recent decades in all Nordic countries, varying from 0.43/100,000 person-years in Sweden and Denmark to 0.65/100,000 person-years in Finland during 2003-2007 (Figure 1) (4). The 5-year survival rate has varied between 22% and 87% over times and regions (5-6).

The aetiology of PFTC is largely unknown, although some risk factors have been identified: high parity decreases the risk, and previous sterilization may be protective (7-9), while chronic infections have not been confirmed as a predisposing factor for this carcinoma (11-12). In Finland, the incidence of PFTC is higher in urban areas than in rural, and almost twice as common among women in the higher social classes as compared to women in the lowest social classes (2). A Finnish study (2) suggested that in 1971-1995 women employed as hairdressers, nurses, private secretaries, book-keepers and accountants had elevated risks for PFTC, but the numbers of cases were small precluding any firm conclusions. The present study is an extension of the previous study on occupation and risk of PFTC (2), including data from all Nordic countries as well as more recent follow up.

Subjects and Methods

The study cohort consists of women aged 30-64 years participating in the 1960, 1970, 1980/1981 and /or 1990 censuses in Denmark, Finland, Iceland, Norway and Sweden and still alive and living in the respective countries on January 1 in the year following the census. All persons were given unique personal identity codes in Sweden in 1947, in Iceland in 1953, in Norway in 1964, in Finland in 1967

and in Denmark in 1968. These codes were used to link census data with cancer data. National cancer registration started in 1943 in Denmark, in 1953 in Finland and Norway, in 1955 in Iceland, and in 1958 in Sweden. In Sweden and Norway, the computerized registration of census data by personal identity codes started in 1960, whereas in Denmark and Finland the first computerised data are available from 1970 census and in Iceland only for the year 1981. Census questionnaires included questions related to persons' economic activity, occupation, and industry. All questionnaires were centrally coded and computerized in the national statistical offices.

In Finland, Norway and Sweden, occupation was coded according to national adaptations of the International Standard Classification of Occupations (ISCO) (usually abbreviated to NYK; Nordisk Yrkesklassifikajon) from 1958, with more than 300 categories. Occupation was coded in Iceland according to a national adaptation of ISCO-68. In Denmark, occupation was coded according to a special national nomenclature with a distinction between self-employed persons, family workers, salaried employees, skilled workers, and unskilled workers; a total of 218 categories. Entities similar to those used in NYK were formed by combining these occupational codes with the 245 codes for industry. For the present study, the original national occupational codes were converted to a common classification with 53 relatively specific, but not too narrow, occupational categories, and an additional category of economically inactive persons (Table 1). Occupational classification in this study is based on the occupation recorded in the first census the person participated in the age range of 30-64 years.

The female population that entered the cohort was followed-up for PFTC incidence during the period from January 1 of the year after the first available census through emigration, death, or to December 31 of the following years: in Denmark 2003, in Finland 2005, in Iceland 2004, in Norway 2003 and in Sweden 2005. The sources of data for death and emigration were the national population registers.

The results are presented as standardized incidence ratios (SIRs) with the cancer incidence rates for the entire national study populations used as reference rates. SIR is counted as the ratio of observed (Obs) and expected numbers of cases. Exact 95% confidence intervals were defined for SIRs with less than 100 observed cases by assuming a Poisson distribution for the observed cases. When the number of observed cases was $\geq$ 100, the confidence intervals were calculated based on a normal approximation to the Poisson distribution. Although SIR calculations were based on 5-year categories of both calendar periods and age, we have here combined the results to 15 year periods and broad age groups of 30-49, 50-64 and 65+ years. The study has been approved by the ethical committee and data inspections boards in each country.

Results

There were 7.5 million women included in the cohort; 3.4 million from Sweden, 1.7 million from Finland, 1.3 million from Norway, 1.0 million from Denmark and 60,000 from Iceland. The number of person-years accumulated by the end of follow up was 200 million. The mean length of follow-up was 26.8 years.

During the follow up, 2206 PFTC cases were detected: 884 in Sweden, 571 in Finland, 384 in Denmark, 358 in Norway and 9 in Iceland. The incidence of PFTC was highest among smelting workers (SIR 3.99, 95% CI 1.46-8.68), artistic workers (2.64, 1.44-4.43) and hairdressers (2.18, 1.41-3.22). Significantly elevated risks for PFTC were also found among packers, nurses, shop workers and clerical workers (Table 1). Non-significantly elevated risks were detected among women working as welders, printers, painters and chemical process workers. Decreased SIRs were discovered among farmers (0.68, 0.47-0.95) and economically inactive women (0.88, 0.82-0.94). The SIR for PFTC sustained quite consistent over time periods among smelting workers, artistic workers, hairdressers,

nurses, chemical process workers as also shop workers and clerical workers (Table 1). There were a slightly decreasing trend over time for the risk of PFTC among hairdressers, smelting workers, chemical process workers and shop and clerical workers but the differences between the period-specific rates were not statistically significant. The SIR among packers in 1991-2005 was significantly lower than before the 1990s. Among farmers the incidence of PFTC was lower than the population average during the period 1976-2005 and among the economically inactive women during the whole study period. We made stratification according to both age and period of diagnosis, but the numbers of cases were too small for identification of significant trends. We tried to evaluate the consistence of the risk for PFTC in different occupations across different Nordic countries (Table 2). The only occupations with consistent risk were hairdressers and nurses.

Discussion

Primary Fallopian tube carcinoma is an uncommon cancer. We present the largest study published so far on occupational risk for PFTC. We found an increased risk for PFTC among smelting workers, artistic workers, hairdressers, nurses, printers, painters, chemical process workers, packers, shop workers and clerical workers. A decreased risk was observed for farmers and economically inactive women.

The strengths of the present study are the relatively large number of cases – the largest study by now, with 45 years of follow-up, reliable diagnoses with virtually full coverage of cancer cases (13-17), and the high accuracy of the occupational codes (18). The linkage between the census data, the mortality and emigration data and the cancer incidence data was based on the unique personal identity codes used in all these registers in all Nordic countries. Since errors in the identifiers are rare (19), the method ensured a complete ascertainment of relevant events.

In the present study, the information on occupations was based on national censuses from 1960-1990. As discussed in detail in Pukkala et al (18), the validity studies indicate that the classification by occupation in the Nordic censuses has been reasonably accurate, but that economic activity has been somewhat underestimated, especially among the women. Occupational classification in this study is based on the occupation recorded in the first census the person participated in the age range of 30-64 years. The extent to which the first census occupation reflects the lifetime experience varies considerably across occupational categories. The occupation at one point in time may not always correspond to the lifelong occupational history of a person. However, comparison with results of special occupational cancer studies indicates that the risk diluting effect of misclassification is small (20-22). The occupational stability proportion of individuals who had the same occupational category (of the 53 categories defined for the present study) in the first and second census available, i.e., 1960 and 1970 censuses in Norway and Sweden, and 1970 and 1980 censuses in Finland was estimated and is described in detail in Pukkala et al (18). In general, in that study stability was higher among men than women and highest in occupational categories where a long education is required such as physicians, dentists and teachers. Nurses were more likely to keep their occupation than assistant nurses, except in Sweden, where female assistant nurses also had a high rate of staying in the occupation. Hairdressers in all countries and of both genders tended to remain in the occupation.

In the present analysis we were unable to take into account the role of potential confounding factors related to PFTC such as parity, breast feeding, sterilization history, previous use of contraceptive pills or hormone replacement therapy or family history of breast and ovarian cancer. Parity strongly protects against PFTC, and the protection increases with increasing number of deliveries (7, 9). Among women in occupations that require high education, mean age at first birth is higher than in women working in other occupational branches, and the total number of pregnancies and deliveries is probably smaller

than, for example, among women working in occupations requiring shorted training periods, such as farming. In the Nordic countries the fertility rates in different socio-economic classes are quite alike. In studies from Norway, Finland, Denmark and Sweden, a similar pattern of lower fertility rates in occupations that require high education and a longer studying period has been detected (18, 23-25). The number of children was also lower among women with higher education and typically the age at first birth is higher. For example, in Norway 16% of physicians are nulliparous, whereas only 6.5% of farmers had no children. In Norway the age at first birth among physicians was 28 years of age and the number of children 2.1, whereas among farmers the corresponding numbers were 23 years of age and the number of children was 3.0 (18). The corresponding numbers for economically inactive women were 24 years of age and the number of children 2.5 (18). In a Finnish survey from 1985 including women aged 40-49, a similar fertility pattern was detected (23). In our study the risk for PFTC was not higher among women in occupations requiring high educations but a lowered risk among farmers was detected. This risk reduction may be in part explained by the effect of higher parity. In the study by Jordan et al. relationship with contraceptive use and breast feeding on the risk of PFTC was studied and a small inverse effect was seen (9). The only studies analyzing the risk of PFTC after a sterilization procedure suggest a non-significant risk reducing effect of this procedure (7,9). These confounding factors might have a minor effect on our results, but it is implausible that they would change our results. The only study analyzing the risk of PFTC after a sterilization procedure is from Finland and suggests a risk reducing effect of this procedure in univariate analysis, but the effect vanished in multivariate analysis (7). To evaluate the possible confounding effect of a previous sterilization procedure we did a search of the commonness of this procedure between the years 1996 and 2008 in different social classes in Finland (www.thl.fi; www.stat.fi). The frequency of this procedure was more common in lower social classes. If an earlier sterilization would confound our results, the lowered risk of PFTC for farmers would be too low. As among hairdressers an earlier sterilization procedure has

been more common, the real risk for PFTC would be even higher than was detected. The same effect would be among smelting workers. Among women in higher social classes the sterilization procedure has been rarer, thus the detected risk estimate for PFTC among nurses might have been too high.

We were unable to take into account the confounding effect of family history of breast and ovarian cancer i.e. the effect of germline BRCA mutations among PFTC patients. A previous study of PFTC discovered that almost one third of PFTC patients have a BRCA germline mutation background, the highest proportions being among younger PFTC patients (26). It is not likely that the BRCA carriers would have been clustered in any specific occupational categories, and therefore we do not consider genetic factors to confound our results. Postmenopausal hormone therapy may be associated with an increase in the risk of PFTC (8, 9). The scarce data available on use of postmenopausal hormone therapy in the Nordic countries or other countries suggest that the selection between the population subcategories is nevertheless rather small and the variation between different educational levels has disappeared (27-30).

We observed an elevated PFTC risk for women working as smelters in particular in Finland and Sweden. Smelting workers may be exposed to nickel, aluminium, arsenic, lead, iron, cadmium or chromium. There are no previous studies of the risk of PFTC among smelting workers other than the one from Finland (2); the material of which is included in the present study, thus no comparison of our results with others is possible. An Italian study reported an increased risk of ovarian cancer among metal workers (31), while in the study by Pukkala et al a similar risk increase was *not* detected for ovarian cancer in Nordic countries (18). Our results may, thus, reflect a real occupational exposure as a risk especially for PFTC for female workers in smelting factories.

The overrepresentation of PFTC among artistic workers in our study could be, at least partly, an effect of exposure to chemical agents as the trend was increasing by age. The dose-response risks related to specific exposure agents will be evaluated in our forthcoming study.

The cancer risk among hairdressers has been widely examined, as hair dyes may contain a variety of carcinogenic agents such as aromatic amines (32). For female hairdressers an elevated risk for cancers of the pancreas, lung, cervix and in situ cancer of the skin was detected in a Swedish cohort study (33). For gynaecological cancers, elevated risks among hairdressers have been observed especially for ovarian and cervical cancer (33-36). In contrast to the results of most of the studies, Shields et al. reported that hairdressers and beauticians were not at increased risk for ovarian cancer (37). We observed a decreasing risk of PFTC with calendar time similar to what has been earlier detected for ovarian cancer in Finland (34). This change in PFTC cancer risk pattern may be due to changed working conditions in hairdressing salons as for decreased use of carcinogenic dyes and hence might be an indication of a real occupational (historical) exposure (34).

As among nurses, a significant increase in risk for PFTC was observed consistently over the years, it is possible that part of risk could be explained by occupational exposures. Earlier studies indicated that nurses exposed to chemotherapeutic drugs were found to have high concentrations of these drugs in their urine (38). Similar findings were reported for health care workers exposed to chemotherapeutic agents, as well as to radiation and viruses (39-40). A study of cancer incidence among a cohort of female Danish nurses observed an increased risk for breast, central nervous system and skin cancer and a decreased risk for alcohol- and tobacco-related cancers (41). In the data by Pukkala et al (18) the risk for ovarian cancer among nurses in Nordic countries was not elevated. Some other epidemiologic investigations of cancer risk among nurses reported excess of ovarian cancer (42-44), but most reports – as ours – have lacked data of confounding factors as parity and lifestyle factors (45).

We observed an elevated risk for PFTC among packers, shop workers and clerical workers. An elevated risk for ovarian cancer has been reported by Shields et al (37) among paper and packaging workers. Our earlier study (2) suggested an increased risk for PFTC among clerical workers from Finland; the additional data in this study included 35 observed PFTC cases vs. 22 expected cases with a SIR of 1.60 between time periods 1971-1995. The decreasing trend of risk of PFTC among clerical and shop workers could reflect an effect of an earlier occupational exposure, followed by a reduction in exposure levels. There was a lowered risk for PFTC among farmers and economically inactive women. Some of the lowered risk of PFTC among farmers – and to a lesser extent among economically inactive women – may be due to the effect of parity (46).

Primary Fallopian tube carcinoma has been very sparsely investigated. Our data covers time period of 45 years. Diagnostic criteria and accuracy may have changed during these years as regards PFTC as also attentiveness of pathologists in classifying between ovarian cancer and PFTC even when small biopsies are available. From the year 2003 new criteria of Tavassoli have been used for PFTC diagnosis (47). It may be that earlier PFTC were misdiagnosed as ovarian cancer, as the cancer that had already spread to adjacent organs in the pelvis was rather diagnosed to be ovarian cancer than PFTC. Because likelihood of such misdiagnosis was similar in all occupations, it should not have affected our relative risk estimates. The reason, why we compare our findings of PFTC with those to results concerning ovarian cancer is the morphological similarity of those two cancers. Ovaries and fallopian tubes are both derived from coelomic epithelium and it has been suggested that serous ovarian carcinomas actually could originate from the fallopian tube mucosa by seeding of disseminated cancer cells from fallopian tube (48). These two cancers also behave and are treated in similar ways.

There are no earlier studies concerning occupation and the risk of PFTC other than our previous study of this subject in Finland (2). The data of this previous study are included in the present Finnish data. In

conclusion, there are women working in certain occupations which are associated with an increased risk for PFTC, especially women working as smelting workers, artists, hairdressers, nurses, clerical and shop workers and packers. Women working as farmers and those who are economically inactive are at decreased risk for PFTC which may reflect the effect of high parity. As we had no individual level information on important potential confounding factors, such as reproductive history, we cannot rule out that these associations may be in part due to confounding. Validation of the present results would require access of data on histories of exposures to occupational, environmental and lifestyle factors, which are planned to be the following steps to be attempted by our research group.

Acknowledgement

This study was supported by grants from Research Funds of Helsinki University Central Hospital and the Finnish Medical Foundation

References

1. Baekelandt M, Jorunn Nesbakken A, Kristensen GB, Trope CG, Abeler VM. Carcinoma of the Fallopian tube. Cancer 2000;89:2076-84.
2. Riska A, Leminen A, Pukkala E. Sociodemographic determinants of incidence of primary Fallopian tube carcinoma, Finland 1953-97. Int J Cancer 2003;104:643-5.
3. Rosenblatt KA, Weiss NS, Schwartz SM. Incidence of malignant Fallopian tube tumours. Gynecol Oncol 1989;35:236-9.
4. Engholm G, Ferlay J, Christensen N, Bray F, Gjerstorff ML, Klint Å, Køtlum JE, Ólafsdóttir E, Pukkala E and Storm HH. NORDCAN: Cancer incidence, mortality, prevalence and prediction in the Nordic countries, Version 3.6 (April 2010). Association of the Nordic Cancer Registries. Danish Cancer Society 2010: http://www.ancr.nu.
5. Benoit MF, Hannigan EV. A 10-year review of primary Fallopian tube cancer at a community hospital: A high association of synchronous and metachronous cancers. Int J Gynecol Cancer 2006;16:29-35.
6. Gadducci A, Landoni F, Sartori E, Maggino T, Zola P, Gabriele A, Rossi R, Cosio S, Fanucchi A, Tisi G. Analysis of treatment failures and survival of patients with Fallopian tube carcinoma: A cooperation task force (CTF) study. Gynecol Oncol 2001;81:150-9.
7. Riska A, Sund R, Pukkala E, Gissler M, Leminen A. Parity, tubal sterilization, hysterectomy and risk of primary Fallopian tube carcinoma in Finland, 1975-2004. Int J Cancer 2007;120:1351-4.
8. Vicus D, Finch A, Rosen B, Fun I, Bradley L, Cass I, Sun P, Karlan B, McLaughlin J, Narod SA and Hereditary Ovarian Cancer Clinical Study Group. Risk factors for carcinoma of the fallopian tube in women with and without a germline BRCA mutation. Gynecol Oncol 2010;118:155-159.
9. Jordan S, Green A, Whiteman D, Moore S, Bain C, Gertig D, Webb P; for the Australian Cancer

Group (ovarian cancer) and the Australian Ovarian Cancer Study Group. Serous ovarian, fallopian tube and primary peritoneal cancers: A comparative epidemiologic analysis. Int J Cancer 2008;122:1598-1603.

10. Riska A, Finne P, Alfthan H, Anttila T, Jalkanen J, Sorvari T, Stenman UH, Paavonen J, Leminen A. Past chlamydial infection is not associated with primary Fallopian tube carcinoma. Eur J Cancer 2006;42:1835-8.
11. Riska A, Finne P, Koskela P, Alfthan H, Jalkanen J, Lehtinen M, Sorvari T, Stenman U, Paavonen J, Leminen A. Human papillomavirus infections and primary Fallopian tube carcinoma: A seroepidemiological study. BJOG 2007;114:425-9.
12. Gungor T, Keskin HL, Zergeroglu S, Keskin EA, Yalcin H, Aydogdu T, Kucukozkan T. Tuberculous salpingitis in two of five primary Fallopian tube carcinomas. J Obstet Gynaecol 2003;23:193-5.
13. Teppo L, Pukkala E, Lehtonen M. Data quality and quality control of a population-based cancer registry. Experience in Finland. Acta Oncol 1994;33: 365-9.
14. Larsen IK, Småstuen M, Johannesen TB, Langmark F, Parkin DM, Bray F, Møller B. Data quality at the Cancer Registry of Norway: an overview of comparability, completeness, validity and timeliness. Eur J Cancer 2009;45:1218-31.
15. Barlow L, Westergren K, Holmberg L, Talback M. The completeness of the Swedish Cancer Register: a sample survey for year 1998. Acta Oncol 2009;48:27-33.
16. Storm HH, Manders T, Spørgel P, Bang S, Jensen OM. Cancer incidence in Denmark 1987. Copenhagen (Denmark): Danish Cancer Society [Kræftens Bekæmpelse]; 1990.
17. Vidarsdottir H, Stefansdottir S, Jonsdottir A, Jonasson JG, Trggvadottir L. [Completeness and accuracy of cancer registration in Iceland. Internal report of Icelandic Cancer Registry].

Reykjavik (Iceland): Krabbameinsskra´ I´slands; 2008. In Icelandic.

18. Pukkala E, Martinsen J, Lynge E, Gunnarsdottir H, Sparen P, Tryggvadottir L, Weiderpass E, Kjaerheim K. Occupation and cancer-follow-up of 15 million people in five Nordic countries. Acta Oncol 2009;48:646-790.
19. Pukkala E. Biobanks and registers in epidemiological research on cancer. In: Dillner J, editor. Methods in biobanking. Methods in Molecular Biology. 2011;675:127-164.
20. Meurman LO, Pukkala E, Hakama M. Incidence of cancer among anthophyllite asbestos miners in Finland. Occup Environ Med 1994; 51: 421-5.
21. Lynge E. Dødelighet og erhverv 1970-75. Statistiske undersøgelser [Mortality and occupation 1970-75. Statistical investigations]. Vol 37. Copenhagen (Denmark): Danmarks Statistik; 1979. Danish.
22. Notkola V, Pajunen A, Leino-Arjas P. Occupational mortality by cause in Finland 1971-1991 and occupational mobility. SVT health. Vol 1. Helsinki (Finland): Statisics Finland; 1997.
23. Pukkala E. Cancer risk by social class and occupation. A survey of 109,000 cancer cases among Finns of working age. In: Wahrendorf J, editor. Contributions to epidemiology and biostatistics. Vol 7. Basel (Switzerland): Karger; 1995.
24. Mørkeberg H. Fødslers placering i familiens livsforløb [Child-spacing in the family life cycle]. Socialforskningsinstituttet rapport No. 68. Copenhagen (Denmark): Socialforskningsinstituttet; 1976. In Danish.
25. Hoem B. Lärare föder fler barn [Teachers have more children]. Välfärdsbulletinen No. 3. Stockholm (Sweden): Statistiska centralbyrån; 1994. p. 17-9. In Swedish.
26. Vicus D, Finch A, Cass I, Rosen B, Murphy J, Fan I, Royer R, McLaughlin J, Karlan B, Narod SA: Prevalence of BRCA1 and BRCA2 germ line mutations among women with carcinoma of the fallopian tube. Gynecol Oncol 2010;118:299-302.

27. Manzoli L, Di Giovanni P, Del Luca L, De Aloysio D, Festi D, Capodicasa S, Monastra G, Romano F, Staniscia T. Use of hormone replacement therapy in Italian women aged 50-70. Maturitas 2004;49:241-251.

28.LambertL, Straton J, Knuiman M, Bartholomew H. health status of users of Hormone replacement therapy by hysterectomy status in Western Australia. J Epidemiol Community Health 2003;57:294-300.

29.Topo P, Luoto R, Hemminki E, Uutela A. Declining socioeconomic differences in the use of menopausal and postmenopausal hormone therapy in Finland. Maturitas 1999;32:141-145.

30.Topo P, Koster A, Holte A, Collins A, Landgren BM, Hemminki E, Uutela A. Trends in the use of climacteric and postclimacteric hormones in Nordic countries. Maturitas 1995,22:89-95.

31. Costantini AS, Pirastu R, Lagorio S, Miligi L, Costa G. Studying cancer among female workers: Methods and preliminary results from a record-linkage system in Italy. J Occup Med 1994; 36: 1180-6.

32. IARC. Occupational exposures of hairdressers and barbers and personal use of hair colorants, some hair dyes, cosmetic colorants, industrial dyestuffs and aromatic amines. IARC Monographs on the evaluation of carcinogenic risks to humans. Vol 57. Lyon, France: IARC, 1993.

33. Czene K, Tiikkaja S, Hemminki K. Cancer risks in hairdressers: Assessment of carcinogenicity of hair dyes and gels. Int J Cancer 2003; 105:108-12.

34. Pukkala E, Nokso-Koivisto P, Roponen P. Changing cancer risk pattern among Finnish hairdressers. Int Arch Occup Environ Health 1992;64:39-42.

35. Boffetta P, Andersen A, Lynge E, Barlow L, Pukkala E. Employment as hairdresser and risk of ovarian cancer and non-Hodgkin's lymphomas among women. J Occup Med 1994;36:61-5.

36. Vasama-Neuvonen K, Pukkala E, Paakkulainen H, Mutanen P, Weiderpass E, Boffetta P, Shen N, Kauppinen T, Vainio H, Partanen T. Ovarian cancer and occupational exposures in Finland.

Am J Ind Med 1999;36:83-9.

37. Shields T, Gridley G, Moradi T, Adami J, Plato N, Dosemeci M. Occupational exposures and the risk of ovarian cancer in Sweden. Am J Ind Med 2002;42:200-13.
38. Mader RM, Rizovski B, Steger GG, Wachter A, Kotz R, Rainer H. Exposure of oncologic nurses to methotrexate in the treatment of osteosarcoma. Arch Environ Health 1996;51:310-4.
39. Stellman JM, Zoloth SR. Cancer chemotherapeutic agents as occupational hazards: A literature review. Cancer Invest 1986;4:127-35.
40. Hewitt JB, Misner ST, Levin PF. Health hazards of nursing: Identifying workplace hazards and reducing risks. AWHONNS Clin Issues Perinat Womens Health Nurs 1993;4:320-7.
41. Kjaer TK, Hansen J. Cancer incidence among large cohort of female Danish registered nurses. socioeconomic status and sterilization Scand J Work Environ Health 2009;35:446-53.
42. Lie JA, Andersen A, Kjaerheim K. Cancer risk among 43000 Norwegian nurses. Scand J Work Environ Health 2007;33:66-73.
43. Sala M, Dosemeci M, Zahm SH. A death certificate-based study of occupation and mortality from reproductive cancers among women in 24 US states. J Occup Environ Med 1998;40:632-9.
44. Petralia SA, Dosemeci M, Adams EE, Zahm SH. Cancer mortality among women employed in health care occupations in 24 US States, 1984-1993. Am J Ind Med 1999;36:159-65.
45. Shen N, Weiderpass E, Anttila A, Goldberg MS, Vasama-Neuvonen KM, Boffetta P, Vainio HU, Partanen TJ. Epidemiology of occupational and environmental risk factors related to ovarian cancer. Scand J Work Environ Health 1998;24:175-82.
46. Pukkala E, Notkola V. Cancer incidence among Finnish farmers, 1979-93. Cancer Causes Control 1997;8:25-33.
47. Tavassoli FA and Devilee P. (eds): World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Breast and Female Genital Organs. IARC Press:

Lyon 2003.

48. Salvador S, Gilks B, Köbel M, Huntsman D, Rosen B, Miller D. The Fallopian tube: Primary site of most pelvic high-grade serour carcinomas. Int J Gynecol Cancer 2009;19:58-64.

Table 1. Observed number (Obs) and standardized incidence ratio (SIR) for primary Fallopian tube cancer in selected occupational categories in the Nordic countries in 1961-2005, by period. 95%CI = 95% confidence interval. Occupations with < 2 observed cases are excluded.

	1961-1975			1976-1990			1991-2005			Total		
Occupational category	Obs	SIR	95%CI	Obs	SIR	95%CI	Obs	SIR	95%CI	Obs	SIR	95%CI
Technical workers	0	0.00	0.00-6.34	1	0.42	0.01-2.34	6	0.74	0.27-1.60	7	0.63	0.25-1.30
Laboratory	0	0.00	0.00-23.57	1	0.79	0.02-4.41	4	0.84	0.23-2.15	5	0.81	0.26-1.89
Physicians	0	0.00	0.00-29.43	1	1.56	0.04-8.67	2	0.87	0.11-3.14	3	0.98	0.20-2.86
Dentists	1	6.61	0.17-36.81	1	1.60	0.04-8.89	3	1.94	0.40-5.67	5	2.15	0.70-5.02
Nurses	2	0.90	0.11-3.24	17	1.64	0.95-2.62	41	1.49	1.07-2.02	60	1.49	1.14-1.92
Assistant nurses	2	0.74	0.09-2.67	18	1.45	0.86-2.29	35	0.97	0.67-1.34	55	1.07	0.81-1.39
"Other health workers"	0	0.00	0.00-2.58	12	1.62	0.84-2.83	21	1.06	0.65-1.62	33	1.15	0.79-1.61
Teachers	1	0.24	0.01-1.33	19	1.05	0.63-1.63	54	1.01	0.76-1.32	74	0.98	0.77-1.23
Religious workers	0	0.00	0.00-3.54	4	0.83	0.22-2.11	18	0.84	0.50-1.33	22	0.81	0.51-1.22
Artistic workers	1	3.27	0.08-18.23	0	0.00	0.00-2.87	13	3.50	1.86-5.99	14	2.64	1.44-4.43
Journalists	0	0.00	0.00-31.18	0	0.00	0.00-6.88	2	1.08	0.13-3.90	2	0.80	0.10-2.88
Administrators	2	1.99	0.24-7.19	5	1.18	0.38-2.74	10	1.07	0.51-1.96	17	1.16	0.68-1.86
Clerical workers	22	1.67	1.05-2.53	71	1.16	0.91-1.46	178	1.18	1.02-1.36	271	1.20	1.07-1.35
Sales agents	0	0.00	0.00-1.69	9	1.50	0.69-2.85	9	0.66	0.30-1.25	18	0.82	0.49-1.30
Shop workers	24	2.20	1.41-3.27	50	1.17	0.87-1-.54	85	1.14	0.92-1.43	159	1.25	1.07-1.46
Farmers	4	0.96	0.26-2.45	12	0.56	0.29-0.99	18	0.73	0.43-1.16	34	0.68	0.47-0.95
Gardeners	5	0.97	0.32-2.28	18	0.76	0.45-1.20	35	0.84	0.59-1.17	58	0.82	0.63-1.07
Transport workers	0	0.00	0.00-21.38	2	3.10	0.38-11.19	2	1.31	0.16-4.72	4	1.70	0.46-4.36
Drivers	0	0.00	0.00-15.51	1	0.90	0.02-5.01	2	0.69	0.08-2.48	3	0.70	0.15-2.05
Postal workers	3	1.29	0.27-3.76	10	1.13	0.54-2.08	25	1.29	0.84-1.91	38	1.25	0.88-1.71
Textile workers	7	1.02	0.41-2.10	16	0.81	0.46-1.31	35	1.14	0.80-1.59	58	1.01	0.77-1.31
Shoe and leather	0	0.00	0.00-6.56	3	1.69	0.35-4.92	4	1.30	0.35-3.32	7	1.29	0.52-2.66
Smelting workers	1	11.2	0.29-62.90	1	2.41	0.06-13.41	4	4.00	1.09-10.24	6	3.99	1.46-8.68
Mechanics	1	1.12	0.03-6.24	4	1.23	0.34-3.16	6	0.83	0.30-1.80	11	0.96	0.48-1.73
Welders	0	0.00	0.00-209	0	0.00	0.00-30.43	2	4.06	0.49-14.66	2	3.17	0.38-11.44
Electrical workers	3	4.82	1.99-14.08	5	1.87	0.61-4.37	5	0.90	0.29-2.10	13	1.47	0.78-2.52
Wood workers	0	0.00	0.00-9.10	5	2.36	0.77-5.51	6	1.29	0.47-2.80	11	1.53	0.76-2.74
Painters	0	0.00	0.00-60.87	1	3.70	0.09-20.60	2	2.97	0.36-10.71	3	2.98	0.62-8.72
Printers	0	0.00	0.00-6.79	4	2.04	0.56-5.23	7	1.69	0.68-3.49	11	1.66	0.83-2.97
Chemical process	3	6.02	1.24-17.59	2	1.11	0.13-4.02	3	1.08	0.22-3.15	8	1.57	0.68-3.10
Food workers	0	0.00	0.00-1.74	9	1.09	0.50-2.07	16	1.31	0.75-2.13	25	1.11	0.72-1.64
Glass makers etc	2	1.84	0.22-6.64	6	1.50	0.55-3.26	8	1.02	0.44-2.01	16	1.24	0.71-2.01
Packers	5	2.98	0.97-6.96	18	3.01	1.79-4.76	9	0.74	0.34-1.41	32	1.62	1.11-2.29
Engine operators	1	11.9	0.30-66.81	0	0.00	0.00-7.50	2	1.23	0.15-4.44	3	1.36	0.28-3.98
Cooks and stewards	2	0.74	0.09-2.69	10	1.47	0.70-2.70	11	0.89	0.44-1.59	23	1.05	0.67-1.58
Domestic assistants	2	0.34	0.04-1.21	19	1.04	0.62-1.62	40	1.12	0.80-1.52	61	1.02	0.78-1.30
Waiters	3	1.17	0.24-3.41	11	1.35	0.67-2.42	11	0.75	0.37-1.34	25	0.98	0.64-1.45
Building caretakers	10	1.06	0.51-1.94	35	0.87	0.61-1.21	51	0.83	0.62-1.10	96	0.87	0.70-1.06
Hairdressers	3	3.37	0.69-9.84	7	2.15	0.86-4.43	15	2.05	1.15-3.38	25	2.18	1.41-3.22
Launderers	2	1.24	0.15-4.49	8	1.76	0.76-3.47	2	0.38	0.05-1.36	12	1.05	0.54-1.83
"Other workers"	3	0.82	0.17-2.38	14	0.94	0.51-1.58	23	0.89	0.57-1.34	40	0.90	0.64-1.23
Economically inactive	127	0.87	0.73-1.03	306	0.86	0.77-0.96	400	0.89	0.81-0.99	833	0.88	0.82-0.94
All categories	242	1.00	Ref.	737	1.00	Ref.	1227	1.00	Ref.	2206	1.00	Ref.

Table 2. Observed (Obs) number and standardised incidence ratio (SIR) for cancer of the fallopian tube among women by country and occupational category. 95%CI = 95% confidence interval. Reference population is the total Nordic population. Only occupations with increased or decreased risks are shown.

	Denmark			Finland			Iceland			Norway			Sweden			Total		
Occupational category	Obs	SIR	95% CI	Obs	SIR	95% CI	Obs	SIR	95% CI	Obs	SIR	95% CI	Obs	SIR	95% CI	Obs	SIR	95% CI
Nurses	10	1.57	0.75-2.89	24	2.43	1.56-3.62	0	0.00	0.00-11.6	9	1.30	0.59-2.47	17	1.04	0.61-1.67	60	1.51	1.15-1.94
Artistic workers	0	0.00	0.00-7.09	4	2.85	0.78-7.30	0	0.00	0.00-53.5	4	4.60	1.25-11.8	6	2.44	0.90-5.31	14	2.63	1.44-4.41
Clerical workers	54	1.55	1.16-2.02	87	1.55	1.24-1.91	2	1.18	0.14-4.26	38	0.99	0.70-1.36	90	0.97	0.78-1.19	271	1.21	1.07-1.36
Shop workers	28	1.30	0.86-1.88	37	1.31	0.92-1.81	0	0.00	0.00-3.57	29	0.99	0.66-1.42	65	1.42	1.10-1.81	159	1.26	1.08-1.47
Farmers	8	0.53	0.23-1.04	9	0.73	0.33-1.39	1	1.35	0.03-7.52	15	0.92	0.51-1.52	1	0.24	0.01-1.34	34	0.70	0.48-0.98
Smelting workers	0	0.00	0.00-25.6	2	3.84	0.47-13.9	0	0.00	0.00-2269	0	0.00	0.00-33.1	4	5.6	1.53-14.3	6	4.03	1.48-8.77
Packers	0	0.00	0.00-9.17	12	1.58	0.82-2.76	0	0.00	0.00-32.4	6	1.48	0.54-3.22	14	1.91	1.04-3.20	32	1.64	1.12-2.32
Hairdressers	3	1.97	0.41-5.76	8	2.81	1.21-5.54	0	0.00	0.00-65.6	2	1.21	0.15-4.37	12	2.2	1.14-3.84	25	2.17	1.40-3.20
Economically inactive	173	1.05	0.90-1.22	143	0.92	0.78-1.08	1	0.30	0.01-1.67	106	0.79	0.65-0.96	410	0.82	0.74-0.90	833	0.87	0.81-0.93
All 54 categories	384	1.13	1.02-1.25	571	1.14	1.05-1.24	9	0.64	0.29-1.21	358	0.95	0.86-1.05	884	0.91	0.85-0.97	2206	1.00	Ref.

Figure 1. Incidence rates (per 100,000 person-years) of primary Fallopian tube cancer in the Nordic countries, by 5-year period, adjusted for age to the World Standard Population. Tabulation based on NORDCAN data (4).